Giving vancomycin as a continuous infusion

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Benchmarking neonatal anthropometric charts published in the last decade

In a commentary published in this journal, we defined the characteristics that a reliable neonatal anthropometric chart should possess to be of both clinical and epidemiological use. With the aim of assessing to what extent the neonatal charts published in the last decade present such characteristics, we examined the relevant literature published from January 1998 to September 2008.

The search strategy in Medline used the following text words and MeSH terms: [(newborn* OR neonatal*) AND (growth charts OR growth curves OR anthropometric charts OR anthropometric curves OR intrauterine growth charts OR intrauterine growth curves) AND (birthweight OR birth head circumference OR birth length) AND (centile* OR percentile* OR gestational age OR LMP) AND (singleton OR standard* OR reference*) NOT longitudinal]. The PubMed “related articles” function was used to search for other relevant papers not retrieved in the initial search. No language restriction was applied. A total of 43 sets of neonatal charts (a set consisting of all the charts referred to the same target population) was identified. Table 1 summarises the results of our appraisal.

General agreement seems to have been achieved over the debated question whether a neonatal chart should be a reference or a standard, as the large majority (80%) of the charts included in this analysis are a reference (which describes “how growth actually is” in a given population), with the only exclusion being stillbirths and major congenital anomalies, rather than a standard (which indicates “how growth should be”), with the exclusion of all neonates exposed to any known risk factor for intrauterine growth.

About two-thirds of the charts are specific for gender and single pregnancy, whereas only a few of them are specific for parity (primiparae/multiparae), which is a maternal constraint known to affect fetal growth.

In 10 cases, the minimum gestational age considered in the charts is 30 weeks or higher, so these charts are unsuitable for the assessment of many preterm neonates.

Reliable neonatal charts require reliable estimates of gestational age. Unfortunately, in 80% of the studies under examination, gestational age is derived from the reported last menstrual period and not from the ultrasound assessment. In only four papers are both estimates considered.

Reliable neonatal charts require reliable anthropometric measures. Regrettably, only 30% of the surveys meet these requirements. Finally, only three charts were traced using the LMS model. In the absence of a model that takes into account the changes in the skewness of distribution of the anthropometric traits with gestational age, the observed values cannot be transformed into z scores. These are particularly useful when the sizes of neonates of different gestational age are to be compared.

Because of the large methodological heterogeneity underlying the neonatal anthropometric charts examined here, we are unable to assert whether or not the observed anthropometric differences reflect actual differences among populations. This fact constitutes a limitation in the use of these charts mainly for epidemiological aims. A deeper consideration of methodological aspects may improve the quality and usefulness of neonatal charts.

Table 1 Adherence to the characteristics suggested for a reliable neonatal anthropometric chart

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-planned multicentre ad hoc study</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Descriptive reference</td>
<td>36 (84)</td>
</tr>
<tr>
<td>Mono-ethnic population</td>
<td>13 (30)</td>
</tr>
<tr>
<td>Charts specific for gender</td>
<td>31 (72)</td>
</tr>
<tr>
<td>Charts specific for single or multiple pregnancy</td>
<td>33 (77)</td>
</tr>
<tr>
<td>Charts specific for parity</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Reliable gestational age estimation</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Reliable measuring techniques and instruments</td>
<td>13 (30)</td>
</tr>
<tr>
<td>Range of gestational age from 42 to 24 weeks</td>
<td>21 (49)</td>
</tr>
<tr>
<td>or less</td>
<td></td>
</tr>
<tr>
<td>HRY* or LMS method used to trace neonatal charts</td>
<td>4 (9)</td>
</tr>
</tbody>
</table>

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The recent paper advocating “a new dosage schedule” for giving vancomycin in early infancy confirms what others have long said is usually the most appropriate total daily dose for babies of less than 34 weeks’ gestation who are more than a week old, and focuses on the time-dependent rather than the concentration-dependent mode of vancomycin killing. Continuous infusion may prevent the risks of high peaks and low troughs seen with intermittent dosage. However, we disagree with the suggestion that a first loading dose is not necessary. The earlier paper that recommended this same strategy 10 years ago correctly said, “Vancomycin half-life is usually between 3 and 10 h in neonates. The time to reach steady state, which is 4 to 5 times the half-life, might thus be expected to be around 48 h in this specific population. Such a time to reach early bactericidal efficacy appeared too long in many cases of septicaemia.” For this reason, we decided to inject a 7 mg kg−1 loading dose.

The one trial to look at the relative merits of intermittent and continuous infusion, which found no evidence that continuous infusions were better than intermittent infusions in adults, also used a loading dose. The reference used to justify the assertion that a loading dose is not necessary was data presented by poster stating that therapeutic levels were reached within 12 h in much older children, but this overlooks the fact that the half-life is much shorter in 5–10-year-old children than it is in the first few weeks of life and, indeed, also rather shorter than it is adult life.

Failure to give a loading dose where there is clear evidence of septicaemia will leave any young baby dangerously under-treated for many hours. There are reasons for thinking that a continuous infusion may be a useful option when treating meningitis, as the discussion of these issues in the Neonatal Formulary web site argues, but a loading dose is required.
REFERENCES